

REMARKS

Amendments

In Claim 1, the limitation “at least 80%” was deleted, and the limitation “or a polymorphic variant, allelic variant, mutant, interspecies homolog, or conservatively modified variant sequence at least 95% identical to SEQ ID NO:31.” Written support for this limitation in the specification at e.g., page 8, lines 13-14 and page 3, lines 10-26. In addition, the recitation of “SEQ ID NO: 29” in claim 1 was deleted.

Claim 6 was amended so that it is in independent form due to the cancellation of claim 5 from which it originally depended.

New claims 22-36 have been added. These claims are directed to methods of diagnosing or monitoring metastatic colorectal cancer in a patient. The subject matter of these claims is supported by the specification at e.g., page 3, lines 2-10; page 4, lines 1-11; page 9, lines 7-17; page 50, lines 25-30; page 51, lines 24-32; page 52, lines 1-6; page 52, lines 10-12; page 53, lines 25-32; and page 54, lines 8-16.

No new matter is added by any of the above amendments. The Examiner is requested to enter the amendments and reconsider the application.

Objections to the Specification

The Examiner has objected to the numbering of the Tables “1-20A” and “1-20B” as inconsistent. Applicants have amended these tables so that they are numbered consecutively as “20A” and “20B.”

The Examiner has objected to Table 26 as a sequence listing that does not comply with the sequence rules. Applicants believe that they have already amended Table 26 so as to overcome the Examiner’s objection. Applicants respectfully point the Examiner to the “Communication under 37 CFR §§ 1.821-1.825 and Preliminary Amendment” dated October 21, 2002. In that submission, Applicants included an amended version of Table 26, as well as, a formal sequence listing in accordance with 37 CFR §§ 1.821-1.825.

The Examiner has objected to the specification because it contains embedded hyperlinks and/or other forms of browser-executable code. Applicants have amended all occurrences of URLs so that they no longer include the browser-executable code “http://” and therefore do not create an embedded hyperlink.

The Rejections Under 35 U.S.C. § 112 ¶2 Should Be Withdrawn

(a) The Examiner has rejected claims 1-7 as vague and indefinite due to the recitation of “selectively hybridizes” in claim 1. The Examiner specifically objects to the term as relative because it depends on the types of sequences in the reaction mix. Applicants respectfully disagree. Applicants specifically define the term “selectively hybridizes to” as “the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent hybridization conditions when that sequence is present in a complex mixture (e.g., total cellular or library DNA or RNA)” at page 18, lines 8-11. Further, Applicants also define “stringent hybridization conditions.” Applicants assert that one of ordinary skill in the art of hybridization reactions at the time of filing of the present application would understand immediately the metes and bounds of stringent hybridization conditions in a complex mixture of nucleic acids. For example, one of ordinary skill would recognize that this type of hybridization reaction may be carried out in performing gene expression microarray hybridizations as exemplified in the present application. Consequently, Applicants believe that the term “selectively hybridizes” provides a clear and definite metes and bounds to one of ordinary skill in the art reading the present claims. Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

(b) The Examiner has rejected the claims as vague and indefinite due to the recitation of “selectively hybridizes to a sequence at least 80% identical to SEQ ID NO: 29 or 31.” In response, Applicants have deleted “at least 80%” and amended the limitation “or a polymorphic variant, allelic variant, mutant, interspecies homolog, or conservatively modified variant sequence at least 95% identical to SEQ ID NO:31.” Applicants provide written description for this limitation in the specification at e.g., page 8, lines 13-14 and page 3, lines 10-26. Applicants believe that the range of nucleic acid sequence variants encompassed by this limitation is unambiguous and well understood by one of ordinary skill in the art. Consequently, Applicants assert that this phrase clearly defines the metes and bounds of the claim. In view of this amendment, Applicants respectfully request that the Examiner withdraw this rejection.

(c) The Examiner has rejected claims 1 and 5 as vague and indefinite because these claims recited sequences beyond those elected. In response, Applicants have deleted the recitation of SEQ ID NO:29 from the claims. In view of this amendment, Applicants

respectfully request that the Examiner withdraw this rejection.

The Written Description Rejections Under 35 U.S.C. § 112 Should Be Withdrawn in View of the Amendment

The Examiner has rejected claims 1-4 for allegedly failing to comply with the written description requirement because the claims recite “at least 80% identical” and thus, claim subject matter that the Examiner asserts was not described in the specification. In response, Applicants have deleted “at least 80%” and amended the limitation “or a polymorphic variant, allelic variant, mutant, interspecies homolog, or conservatively modified variant sequence at least 95% identical to SEQ ID NO:31.” Applicants believe that the range of nucleic acid sequence variants with 95% identity encompassed by this limitation would be immediately recognized by one of ordinary skill in the art as within the family of genes defined by SEQ ID NO:31. It is this family of related genes that the inventors described in the specification through the detailed description of percentage sequence identity and variants at, e.g., page 8, line 11 through page 9, line 6; page 9, line 24 through page 12, line 3; and page 13, lines 10-26. Thus, Applicants believe that the claims, as amended, do not embrace any sequences that have not been described.

Applicants also wish to address the Examiner’s assertions that the claims cover a large number of sequence permutations (e.g. substitution of up to 241 contiguous nucleotides in the full-length 1208 nucleotide sequence) that would hybridize to sequences not disclosed in the specification. Applicants believe that the current amendment overcomes the Examiner’s rejection. Although 95% identity to SEQ ID NO:31 may include changes to approximately 60 different nucleotides across the full-length (1208 nucleotide) sequence, the types of variants now recited in the claim (e.g. polymorphic variant, allelic variant, mutant, interspecies homolog, or conservatively modified variants) would hybridize only to sequences within the inventor’s possession as evidenced by the disclosure. These types of sequence variants are described in the specification (at, e.g., page 8, line 11 through page 9, line 6; page 9, line 24 through page 12, line 3; and page 13, lines 10-26), and also, were well-known to one of ordinary skill in the art at the time of filing. In view of this amendment, Applicants respectfully request that the Examiner withdraw this rejection.

The Utility Rejection Under 35 U.S.C. § 101 Should Be Withdrawn

The Examiner has rejected claims 1-7 for lacking patentable utility because the

application allegedly fails to disclose “any connection between SEQ ID NO: 31 and colo-rectal cancer.” Applicants respectfully disagree. Applicants wish to point the Examiner to the data disclosed in Table 21 beginning at page 220. Specifically, Table 21 discloses results of screening human gene expression levels in colon cancer derived liver metastases versus normal colon tissue. The Table lists a small set of 310 human genes, out of the 1000s that were screened using the Affymetrix/EosHu03 microarray, that are up-regulated in the colon cancer derived liver metastases. SEQ ID NO:31 (which corresponds to UnigeneID Hs.163900) was found to exhibit an up-regulation ratio of 4.58 as is shown in Table 21 at page 222, line 7. Applicants assert that one of ordinary skill reviewing the gene expression data listed in Table 21 would immediately recognize that it establishes a substantial and credible connection between SEQ ID NO:31 and colorectal cancer. In view of the connection disclosed by the data in Table 21, Applicants respectfully reconsider and withdraw the rejection of claims 1-7 for lack of utility.

The Enablement Rejections Under 35 U.S.C. § 112 Should Be Withdrawn

The Examiner has rejected claims 1-7 for failing to comply with the enablement requirement. Specifically, the Examiner appears to allege that because there is no disclosed connection between SEQ ID NO:31 and colorectal cancer, the claimed methods (claims 1-4), and claimed vector and host cells (claims 5-7) are not enabled. Applicants respectfully disagree and traverse this rejection for the same reasons described above with respect to the lack of utility rejections. Applicants assert that they have disclosed a clear connection between SEQ ID NO:31 and colorectal cancer based on the actual data found in Table 21 of the specification.

Moreover, Applicants’ specification is replete with enabling disclosure regarding methods of using nucleic acid sequences and the encoded polypeptides in assays to detect cancer (see, e.g., section titled, “Detection of metastatic colorectal cancer sequence for diagnostic and therapeutic applications” beginning at page 50 of the specification). Use of the disclosed nucleic acid sequences in vectors and host cells also is described in the specification (see, e.g., section titled “Expression of metastatic colorectal cancer proteins from nucleic acids” beginning at page 37). Applicants assert that one of ordinary skill in the art using this disclosure would be able to make and use the full scope of the claimed invention. Consequently, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

The Rejection Under 35 U.S.C. § 102(a) Is Obviated by Cancellation of Claim 5

The Examiner rejected claim 5 as anticipated by the Hong et al. reference. Applicants have cancelled claim 5 and thereby rendered this rejection moot.

CONCLUSION

Applicants believe that the application is in good and proper condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 463-8133.

Respectfully submitted,

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